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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,596	12/05/2001	Colin Bernard Reese	P 0282829	7915

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EXAMINER

LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 01/22/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/914,596

Applicant(s)

REESE ET AL.

Examiner

Patrick T. Lewis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Applicant's Response dated September 22, 2003

1. In the Response filed September 22, 2003, the specification was amended; the abstract was amended; claims 1-3, 5, and 7-8 were amended; claims 9-14 were added. Applicant presented arguments directed to the rejection of claims 1-2 under 35 U.S.C. 112, first paragraph; the rejection of claims 1-8 under 35 U.S.C. 112, second paragraph; and the rejection of claims 1-6 under 35 U.S.C. 103(a). Claims 1-14 are pending. An action on the merits of claims 1-14 is contained herein below.
2. The objection to claims 7-8 as being in improper multiple dependent forms has been rendered moot in view of applicant's amendment dated September 22, 2003.
3. Applicant's arguments, see pages 11-12, filed September 22, 2003, with respect to the rejection of claims 1-2 under 35 U.S.C. 112, first paragraph, have been fully considered and are persuasive. The rejection of claims 1-2 has been withdrawn.
4. Applicant's arguments/amendment, see pages 8-9 and 13-14, filed September 22, 2003, with respect to the rejection of claims 1-8 under 35 U.S.C. 112, second paragraph, have been fully considered and are persuasive. The rejection of claims 1-8 has been withdrawn.
5. The rejection of claims 1-6 under 35 U.S.C. § 103(a) is maintained for the reasons of record set forth in the Office Action dated May 20, 2003.

Objections/Rejections of Record Set For the in Office Action dated May 20, 2003

6. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al. WO 96/27606 (Cook) in view of McGee et al. *Nucleosides & Nucleotides* (1996), Vol. 15 (11 & 12), pages 1797-1803 (McGee).

Response to Arguments

7. Applicant's arguments filed September 22, 2003, have been fully considered but they are not persuasive.

Applicant argues: 1) the art of record fails to teach using $Al(OR)_3$ as the Lewis acid and 2) the instantly claimed method yields unexpected results.

The examiner disagrees with applicant's characterization of Cook. Contrary to applicant's assertions, Cook does not simply define "Lewis acids". On page 33, Cook teaches that divalent and trivalent hard acids are particularly preferred as the Lewis acid employed process. More particularly, Cook teaches the divalent and trivalent cations of magnesium, calcium, aluminum, zinc, chromium, copper, boron, tin, mercury, iron, manganese, cadmium, gallium and barium. Their complexes include hydroxides, alkyls, alkoxides, di- and trihalides, and organic acid ligands such as acetates. Although Cook only mentions borates with any specificity and in the examples, it would have been obvious to one of ordinary skill in the art at the time of the invention that the teachings of Cook were broad with respect to useful Lewis acids. All of the limitations or absolute predictability is not required to establish *prima facie* obviousness. One of ordinary skill in the art at the time of the invention would have had a reasonable expectation of

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success in employing any one of a wide range of Lewis acids including Al(OR)_3 . As further shown by McGee, it was known in the art at the time of the invention to convert a 2,2'-anhydropyridine nucleoside to a 2'-O-substituted pyrimidine using a variety of Lewis acids. The teachings of Cook and McGee are seen to provide sufficient guidance and motivation for practicing the instantly claimed method. The selection of a known material based on its suitability for its intended use is *prima facie* obvious. In the absence of evidence of a secondary nature to obviate the rejection as set forth in the Office Action dated May 20, 2003, or of some specific limitations which would tip the scale of patentability in the favor of the instantly claimed invention, it would have been obvious to one of ordinary skill in this art at the time of the invention to use a Lewis acid of equivalent or comparable activity to convert the 2,2'-anhydropyrimidine nucleoside to a 2'-O-substituted pyrimidine. Applicant's remarks concerning "unexpected results" have been noted; however, the arguments of counsel cannot take the place of evidence in the record.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al. WO 96/27606 (Cook) in view of McGee et al. *Nucleosides & Nucleotides* (1996), Vol. 15 (11 & 12), pages 1797-1803 (McGee).

Claims 7-14 are drawn to a process for the preparation of 2'-O-substituted nucleosides, and in particular, 2'-O-substituted uridines, by reacting a tris-substituted aluminum with a 2'-leaving group.

Cook teaches a process for the synthesis of 2'-O-substituted pyrimidines and oligomeric compounds therefrom. See Abstract. On page 9, line 35 to page 10, line 16, Cook discloses the synthesis of 2'-O-substituted pyrimidines via a reaction of the corresponding 2-2'-anhydropyrimidine nucleoside with a Lewis acid. Further, on page

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11, lines 12-18, Cook teaches that the methodology can be used for the preparation of 2'-O-substituted uridines, which can be aminated to give a 2'-O-substituted cytidine. On page 33, lines 11-27, Cook teaches that the Lewis acid is preferably the di- or trivalent cations of di- and trivalent metals, including magnesium, calcium, aluminum, zinc, chromium, copper, boron, tin, mercury, iron, manganese, cadmium, gallium and barium, and their complexes, including alkoxides. Procedure 3 of Example 20 (page 46) teaches a conversion using tri-alkyl borate with 100% yield and 97% purity.

Cook does not explicitly teach tris-O-substituted aluminum as the Lewis acid.

McGee teaches a process for the synthesis of 2'-O-substituted uridine via a reaction of the corresponding 2-2'-anhydrouridine with magnesium or calcium alkoxide. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use any one of the disclosed Lewis acid of Cook for the conversion of 2-2'-anhydropyrimidine nucleoside to a 2'-O-substituted pyrimidine, including a tris-O-substituted aluminum, as it is known in the art that several of the disclosed Lewis acids, namely magnesium and calcium alkoxide or McGee, and tri-alkyl borate of Cook, are effective for such reactions. A skilled artisan would have been motivated and would have had a reasonable expectation of success to use a Lewis acid of equivalent or comparable activity to convert the 2-2'-anhydropyrimidine nucleoside to a 2'-O-substituted pyrimidine.

Conclusion

12. Claims 1-14 are pending. Claims 1-14 are rejected. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis, PhD
Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
January 19, 2004